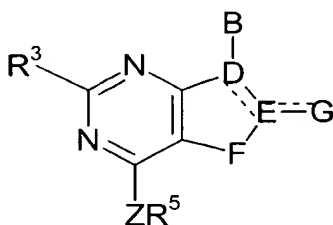


18. A compound of the formula



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wherein the dashed lines represent optional double bonds;

B is $-NR^1R^2$, $-CR^1R^2R^{10}$, $-C(=CR^2R^{11})R^1$, $-NHCR^1R^2R^{10}$, $-OCR^1R^2R^{10}$, $-SCR^1R^2R^{10}$, $-CR^2R^{10}NHR^1$, $-CR^2R^{10}OR^1$, $-CR^2R^{10}SR^1$ or $-COR^2$;

E is nitrogen, CH or carbon;

D is nitrogen and is single bonded to all atoms to which it is attached, or D is carbon and is double bonded to E, or D is CH and is single bonded to E;

F is CHR^4 or NR^4 ; provided that at least one of D and E is nitrogen or F is NR^4 , and provided that only one of D and E is nitrogen, and D and E are not nitrogen when F is NR^4 ;

G, when single bonded to E, is hydrogen, C_1 - C_4 alkyl, $-S(C_1$ - C_4 alkyl), $-O(C_1$ - C_4 alkyl), NH_2 , $-NH(C_1$ - C_4 alkyl) or $-N(C_1$ - C_2 alkyl)(C_1 - C_4 alkyl), wherein each of the C_1 - C_4 alkyl groups of G may optionally be substituted with one hydroxy, $-O(C_1$ - C_2 alkyl) or fluoro group; and G, when double bonded to E, is oxygen, sulfur or NH; and G, when E is nitrogen and double bonded to D, is absent;

R^1 is hydrogen, C_1 - C_6 alkyl optionally substituted with one or two substituents R^8 independently selected from hydroxy, fluoro, chloro, bromo, iodo, C_1 - C_4 alkoxy, CF_3 , $-C(=O)O$ -(C_1 - C_4)alkyl, $-OC(=O)(C_1$ - C_4 alkyl), $-OC(=O)N(C_1$ - C_4 alkyl)(C_1 - C_2 alkyl), $-NHCO(C_1$ - C_4 alkyl), $-COOH$, $-COO(C_1$ - C_4 alkyl), $-CONH(C_1$ - C_4 alkyl), $-CON(C_1$ - C_4 alkyl)(C_1 - C_2 alkyl), $-S(C_1$ - C_4 alkyl), $-CN$, $-NO_2$, $-SO(C_1$ - C_4 alkyl), $-SO_2(C_1$ - C_4 alkyl), $-SO_2NH(C_1$ - C_4 alkyl) and $-SO_2N(C_1$ - C_4 alkyl)(C_1 - C_2 alkyl), wherein a carbon-carbon single bond of each of the C_1 - C_4 alkyl groups in the foregoing R^1 groups having at least two carbons may optionally be replaced with a carbon-carbon double or triple bond, and one or two carbon-carbon single bonds of each of the C_1 - C_4 alkyl groups in the foregoing R^1 groups having four carbons may optionally be replaced with a carbon-carbon double or triple bond; R^2 is C_1 - C_{12} alkyl wherein one carbon-carbon single bond of any said alkyl having at least two carbons, one or two carbon-carbon single bonds of any said alkyl having at least four carbons, and from one to three carbon-carbon single bonds of any said

alkyl having at least six carbons may optionally be replaced with a carbon-carbon double or triple bond, or R^2 is aryl or $(C_1-C_4 \text{ alkylene})\text{aryl}$, wherein said aryl and the aryl moiety of said $(C_1-C_4 \text{ alkylene})\text{aryl}$ is selected from phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidinyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl, isothiazolyl, pyrazolyl, pyrrolyl, indolyl, pyrrolopyridyl, oxazolyl and benzoxazolyl; or R^2 is C_3-C_8 cycloalkyl or $(C_1-C_6 \text{ alkylene})(C_3-C_8 \text{ cycloalkyl})$, wherein one or two of the carbon atoms of said cycloalkyl and the 5 to 8 membered cycloalkyl moieties of said $(C_1-C_6 \text{ alkylene})(C_3-C_8 \text{ cycloalkyl})$ may optionally and independently be replaced by an oxygen or sulfur atom or by NZ^2 wherein Z^2 is selected from hydrogen, C_1-C_4 alkyl, benzyl and C_1-C_4 alkanoyl, and wherein each of the foregoing R^2 groups may optionally be substituted with from one to three substituents independently selected from chloro, fluoro, hydroxy and C_1-C_4 alkyl, or with one substituent selected from bromo, iodo, C_1-C_6 alkoxy, $-OC(=O)(C_1-C_6 \text{ alkyl})$, $-OC(=O)N(C_1-C_4 \text{ alkyl})(C_1-C_2 \text{ alkyl})$, $-S(C_1-C_6 \text{ alkyl})$, amino, $-NH(C_1-C_2 \text{ alkyl})$, $-N(C_1-C_2 \text{ alkyl})(C_1-C_4 \text{ alkyl})$, $-N(C_1-C_4 \text{ alkyl})-CO-(C_1-C_4 \text{ alkyl})$, $-NHCO(C_1-C_4 \text{ alkyl})$, $-COOH$, $-COO(C_1-C_4 \text{ alkyl})$, $-CONH(C_1-C_4 \text{ alkyl})$, $-CON(C_1-C_4 \text{ alkyl})(C_1-C_2 \text{ alkyl})$, $-SH$, $-CN$, $-NO_2$, $-SO(C_1-C_4 \text{ alkyl})$, $-SO_2(C_1-C_4 \text{ alkyl})$, $-SO_2NH(C_1-C_4 \text{ alkyl})$ and $-SO_2N(C_1-C_4 \text{ alkyl})(C_1-C_2 \text{ alkyl})$;

$-NR^1R^2$ or $-CR^1R^2R^{10}$ may form a 3 to 8 membered ring consisting of single bonds, wherein one or two of the ring carbon atoms of such a 5 to 8 membered ring may optionally and independently be replaced by an oxygen or sulfur atom or by NZ^3 wherein Z^3 is hydrogen, C_1-C_4 alkyl, benzyl or C_1-C_4 alkanoyl, and wherein from one to three of the single bonds of such a 3 to 8 membered ring that are carbon-carbon or carbon-nitrogen single bonds may each optionally be replaced with a double bond;

R^3 is hydrogen, C_1-C_4 alkyl, $-O(C_1-C_4 \text{ alkyl})$, chloro, fluoro, bromo, iodo, $-CN$, $-S(C_1-C_4 \text{ alkyl})$ or $-SO_2(C_1-C_4 \text{ alkyl})$ wherein each of the $(C_1-C_4 \text{ alkyl})$ moieties in the foregoing R^3 groups may optionally be substituted with one substituent R^9 selected from hydroxy, fluoro and $(C_1-C_2 \text{ alkoxy})$;

each R^4 is, independently, hydrogen, $(C_1-C_6 \text{ alkyl})$, fluoro, chloro, bromo, iodo, trifluoromethyl, hydroxy, cyano, amino, nitro, $-O(C_1-C_4 \text{ alkyl})$, $-N(C_1-C_4 \text{ alkyl})(C_1-C_2 \text{ alkyl})$, $-S(C_1-C_4 \text{ alkyl})$, $-SO(C_1-C_4 \text{ alkyl})$, $-SO_2(C_1-C_4 \text{ alkyl})$, $-CO(C_1-C_4 \text{ alkyl})$, $-C(=O)H$ or $-C(=O)O(C_1-C_4 \text{ alkyl})$, wherein one or two of the carbon-carbon single bonds in each of the $(C_1-C_6 \text{ alkyl})$ and $(C_1-C_4 \text{ alkyl})$ moieties in the foregoing R^4 groups may optionally be replaced with a carbon-carbon double or triple bond and wherein each of said $(C_1-C_6 \text{ alkyl})$ and $(C_1-C_4 \text{ alkyl})$ moieties

may optionally be substituted with one or two substituents independently selected from hydroxy, amino, C₁-C₃ alkoxy, dimethylamino, methylamino, ethylamino, -NHC(=O)CH₃, fluoro, chloro, C₁-C₃ alkylthio, -CN, -COOH, -C(=O)O(C₁-C₄ alkyl), -C(=O)(C₁-C₄ alkyl) and -NO₂;

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cont

R⁵ is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, furanyl, benzofuranyl, benzothiazolyl, benzisothiazolyl, benzisoxazolyl, benzimidazolyl, indolyl, benzoxazolyl or C₃-C₈ cycloalkyl wherein one or two of the carbon atoms of said cycloalkyl rings that contain at least 5 ring members may optionally and independently be replaced by an oxygen or sulfur atom or by NZ⁴ wherein Z⁴ is hydrogen, C₁-C₄ alkyl or benzyl; and wherein each of the foregoing R⁵ groups is substituted with from one to four substituents wherein one to three of said substituents may be selected, independently, from chloro, C₁-C₆ alkyl and -O(C₁-C₆ alkyl) and one of said substituents may be selected from bromo, iodo, formyl, -CN, -CF₃, -NO₂, -NH₂, -NH(C₁-C₄ alkyl), -N(C₁-C₂ alkyl)(C₁-C₆ alkyl), -C(=O)O(C₁-C₄ alkyl), -C(=O)(C₁-C₄ alkyl), -COOH, -SO₂NH(C₁-C₄ alkyl), -SO₂N(C₁-C₂ alkyl)(C₁-C₄ alkyl), -SO₂NH₂, -NHSO₂(C₁-C₄ alkyl), -S(C₁-C₆ alkyl) and -SO₂(C₁-C₆ alkyl), and wherein each of the C₁-C₄ alkyl and C₁-C₆ alkyl moieties in the foregoing R⁵ groups may optionally be substituted with one or two substituents independently selected from fluoro, hydroxy, amino, methylamino, dimethylamino and acetyl; and furthermore wherein when R⁵ is phenyl or pyridyl substituted with three substituents, said substituents can further be selected from (C₁-C₄ alkyl)O(C₁-C₄ alkyl), OCF₃, and fluoro, and one carbon-carbon single bond of each (C₁-C₄) alkyl group of said substituents having between two and four carbon atoms may be optionally replaced with a carbon-carbon double or triple bond; or R⁵ is pyrimidyl substituted by three substituents independently selected from C₁-C₄ alkyl, -O(C₁-C₄ alkyl), CF₃, OCF₃, -CHO, (C₁-C₄ alkyl)-OH, CN, Cl, F, Br, I and NO₂, wherein a carbon-carbon single bond of said (C₁-C₄) alkyl groups having between two and four carbon atoms may optionally be replaced by a carbon-carbon double or triple bond;

R⁷ is hydrogen, C₁-C₄ alkyl, halo, cyano, hydroxy, -O(C₁-C₄ alkyl) -C(=O)(C₁-C₄ alkyl), -C(=O)O(C₁-C₄alkyl), -OCF₃, -CF₃, -CH₂OH, -CH₂O(C₁-C₄ alkyl);

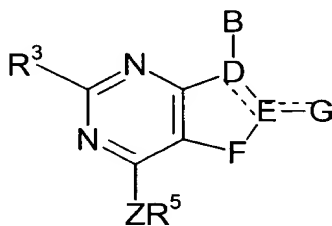
R¹⁰ is hydrogen, hydroxy, methoxy or fluoro;

R¹¹ is hydrogen or C₁-C₄ alkyl; and

with the proviso that: (a) when R⁴ is attached to nitrogen, it is not halo, cyano or nitro; and (b) one of E, D and F must be nitrogen or substituted nitrogen, and only one of E, D and F can be nitrogen or substituted nitrogen;

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Cont Z is NH, oxygen, sulfur, -N(C₁-C₄ alkyl), -NC(=O)(C₁-C₂ alkyl), NC(=O)O(C₁-C₂alkyl) or CR¹³R¹⁴ wherein R¹³ and R¹⁴ are independently selected from hydrogen, trifluoromethyl and methyl with the exception that one of R¹³ and R¹⁴ can be cyano;
or a pharmaceutically acceptable salt of such compound.

25. A compound of the formula



wherein the dashed lines represent optional double bonds;

B is -NR¹R², -CR¹R²R¹⁰, -C(=CR²R¹¹)R¹, -NHCR¹R²R¹⁰, -OCR¹R²R¹⁰, -SCR¹R²R¹⁰, -CR²R¹⁰NHR¹, -CR²R¹⁰OR¹, -CR²R¹⁰SR¹ or -COR²;

E is nitrogen, CH or carbon;

D is nitrogen and is single bonded to all atoms to which it is attached, or D is carbon and is double bonded to E, or D is CH and is single bonded to E;

F is CHR⁴ or NR⁴; provided that at least one of D and E is nitrogen or F is NR⁴, and provided that only one of D and E is nitrogen, and D and E are not nitrogen when F is NR⁴;

G, when single bonded to E, is hydrogen, C₁-C₄ alkyl, -S(C₁-C₄ alkyl), -O(C₁-C₄ alkyl), -NH₂, -NH(C₁-C₄ alkyl) or -N(C₁-C₂ alkyl)(C₁-C₄ alkyl), wherein each of the C₁-C₄ alkyl groups of G may optionally be substituted with one hydroxy, -O(C₁-C₂ alkyl) or fluoro group; and G, when double bonded to E, is oxygen, sulfur or NH; and G, when E is nitrogen and double bonded to D, is absent;

R¹ is hydrogen, C₁-C₆ alkyl optionally substituted with one or two substituents R⁸ independently selected from hydroxy, fluoro, chloro, bromo, iodo, C₁-C₄ alkoxy, CF₃, -C(=O)O-(C₁-C₄)alkyl, -OC(=O)(C₁-C₄ alkyl), -OC(=O)N(C₁-C₄ alkyl)(C₁-C₂ alkyl), -NHCO(C₁-C₄ alkyl), -COOH, -COO(C₁-C₄ alkyl), -CONH(C₁-C₄ alkyl), -CON(C₁-C₄ alkyl)(C₁-C₂ alkyl), -S(C₁-C₄ alkyl), -CN, -NO₂, -SO(C₁-C₄ alkyl), -SO₂(C₁-C₄ alkyl), -SO₂NH(C₁-C₄ alkyl) and -SO₂N(C₁-C₄ alkyl)(C₁-C₂ alkyl), wherein a carbon-carbon single bond of each of the C₁-C₄ alkyl groups in the foregoing R¹ groups having at least two carbons may optionally be replaced with a carbon-

carbon double or triple bond, and one or two carbon-carbon single bonds of each of the C_1-C_4 alkyl groups in the foregoing R^1 groups having four carbons may optionally be replaced with a carbon-carbon double or triple bond; R^2 is C_1-C_{12} alkyl wherein one carbon-carbon single bond of any said alkyl having at least two carbons, one or two carbon-carbon single bonds of any said alkyl having at least four carbons, and from one to three carbon-carbon single bonds of any said alkyl having at least six carbons may optionally be replaced with a carbon-carbon double or triple bond, or R^2 is aryl or $(C_1-C_4 \text{ alkylene})\text{aryl}$, wherein said aryl and the aryl moiety of said $(C_1-C_4 \text{ alkylene})\text{aryl}$ is selected from phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidinyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl, isothiazolyl, pyrazolyl, pyrrolyl, indolyl, pyrrolopyridyl, oxazolyl and benzoxazolyl; or R^2 is C_3-C_8 cycloalkyl or $(C_1-C_6 \text{ alkylene})(C_3-C_8 \text{ cycloalkyl})$, wherein one or two of the carbon atoms of said cycloalkyl and the 5 to 8 membered cycloalkyl moieties of said $(C_1-C_6 \text{ alkylene})(C_3-C_8 \text{ cycloalkyl})$ may optionally and independently be replaced by an oxygen or sulfur atom or by NZ^2 wherein Z^2 is selected from hydrogen, C_1-C_4 alkyl, benzyl and C_1-C_4 alkanoyl, and wherein each of the foregoing R^2 groups may optionally be substituted with from one to three substituents independently selected from chloro, fluoro, hydroxy and C_1-C_4 alkyl, or with one substituent selected from bromo, iodo, C_1-C_6 alkoxy, $-\text{OC}(=\text{O})(C_1-C_6 \text{ alkyl})$, $-\text{OC}(=\text{O})\text{N}(C_1-C_4 \text{ alkyl})(C_1-C_2 \text{ alkyl})$, $-\text{S}(C_1-C_6 \text{ alkyl})$, amino, $-\text{NH}(C_1-C_2 \text{ alkyl})$, $-\text{N}(C_1-C_2 \text{ alkyl})(C_1-C_4 \text{ alkyl})$, $-\text{N}(C_1-C_4 \text{ alkyl})-\text{CO}-(C_1-C_4 \text{ alkyl})$, $-\text{NHCO}(C_1-C_4 \text{ alkyl})$, $-\text{COOH}$, $-\text{COO}(C_1-C_4 \text{ alkyl})$, $-\text{CONH}(C_1-C_4 \text{ alkyl})$, $-\text{CON}(C_1-C_4 \text{ alkyl})(C_1-C_2 \text{ alkyl})$, $-\text{SH}$, $-\text{CN}$, $-\text{NO}_2$, $-\text{SO}(C_1-C_4 \text{ alkyl})$, $-\text{SO}_2(C_1-C_4 \text{ alkyl})$, $-\text{SO}_2\text{NH}(C_1-C_4 \text{ alkyl})$ and $-\text{SO}_2\text{N}(C_1-C_4 \text{ alkyl})(C_1-C_2 \text{ alkyl})$;

$-\text{NR}^1\text{R}^2$ or $-\text{CR}^1\text{R}^2\text{R}^{10}$ may form a 3 to 8 membered ring consisting of single bonds, wherein one or two of the ring carbon atoms of such a 5 to 8 membered ring may optionally and independently be replaced by an oxygen or sulfur atom or by NZ^3 wherein Z^3 is hydrogen, C_1-C_4 alkyl, benzyl or C_1-C_4 alkanoyl, and wherein from one to three of the single bonds of such a 3 to 8 membered ring that are carbon-carbon or carbon-nitrogen single bonds may each optionally be replaced with a double bond;

R^3 is hydrogen, C_1-C_4 alkyl, $-\text{O}(C_1-C_4 \text{ alkyl})$, chloro, fluoro, bromo, iodo, $-\text{CN}$, $-\text{S}(C_1-C_4 \text{ alkyl})$ or $-\text{SO}_2(C_1-C_4 \text{ alkyl})$ wherein each of the $(C_1-C_4 \text{ alkyl})$ moieties in the foregoing R^3 groups may optionally be substituted with one substituent R^9 selected from hydroxy, fluoro and $(C_1-C_2 \text{ alkoxy})$;

each R^4 is, independently, hydrogen, (C_1-C_6 alkyl), fluoro, chloro, bromo, iodo, trifluoromethyl, hydroxy, cyano, amino, nitro, $-O(C_1-C_4 \text{ alkyl})$, $-N(C_1-C_4 \text{ alkyl})(C_1-C_2 \text{ alkyl})$, $-S(C_1-C_4 \text{ alkyl})$, $-SO(C_1-C_4 \text{ alkyl})$, $-SO_2(C_1-C_4 \text{ alkyl})$, $-CO(C_1-C_4 \text{ alkyl})$, $-C(=O)H$ or $-C(=O)O(C_1-C_4 \text{ alkyl})$, wherein one or two of the carbon-carbon single bonds in each of the (C_1-C_6 alkyl) and (C_1-C_4 alkyl) moieties in the foregoing R^4 groups may optionally be replaced with a carbon-carbon double or triple bond and wherein each of said (C_1-C_6 alkyl) and (C_1-C_4 alkyl) moieties may optionally be substituted with one or two substituents independently selected from hydroxy, amino, C_1-C_3 alkoxy, dimethylamino, methylamino, ethylamino, $-NHC(=O)CH_3$, fluoro, chloro, C_1-C_3 alkylthio, $-CN$, $-COOH$, $-C(=O)O(C_1-C_4 \text{ alkyl})$, $-C(=O)(C_1-C_4 \text{ alkyl})$ and $-NO_2$;

R^5 is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, furanyl, benzofuranyl, benzothiazolyl, benzisothiazolyl, benzisoxazolyl, benzimidazolyl, indolyl, benzoxazolyl or C_3-C_8 cycloalkyl wherein one or two of the carbon atoms of said cycloalkyl rings that contain at least 5 ring members may optionally and independently be replaced by an oxygen or sulfur atom or by NZ^4 wherein Z^4 is hydrogen, C_1-C_4 alkyl or benzyl; and wherein each of the foregoing R^5 groups is substituted with from one to four substituents wherein one to three of said substituents may be selected, independently, from chloro, C_1-C_6 alkyl and $-O(C_1-C_6 \text{ alkyl})$ and one of said substituents may be selected from bromo, iodo, formyl, $-CN$, $-CF_3$, $-NO_2$, $-NH_2$, $-NH(C_1-C_4 \text{ alkyl})$, $-N(C_1-C_2 \text{ alkyl})(C_1-C_6 \text{ alkyl})$, $-C(=O)O(C_1-C_4 \text{ alkyl})$, $-C(=O)(C_1-C_4 \text{ alkyl})$, $-COOH$, $-SO_2NH(C_1-C_4 \text{ alkyl})$, $-SO_2N(C_1-C_2 \text{ alkyl})(C_1-C_4 \text{ alkyl})$, $-SO_2NH_2$, $-NHSO_2(C_1-C_4 \text{ alkyl})$, $-S(C_1-C_6 \text{ alkyl})$ and $-SO_2(C_1-C_6 \text{ alkyl})$, and wherein each of the C_1-C_4 alkyl and C_1-C_6 alkyl moieties in the foregoing R^5 groups may optionally be substituted with one or two substituents independently selected from fluoro, hydroxy, amino, methylamino, dimethylamino and acetyl;

R^7 is hydrogen, C_1-C_4 alkyl, halo, cyano, hydroxy, $-O(C_1-C_4 \text{ alkyl})$, $-C(=O)(C_1-C_4 \text{ alkyl})$, $-C(=O)O(C_1-C_4 \text{ alkyl})$, $-OCF_3$, $-CF_3$, $-CH_2OH$, $-CH_2O(C_1-C_4 \text{ alkyl})$;

R^{10} is hydrogen, hydroxy, methoxy or fluoro;

R^{11} is hydrogen or C_1-C_4 alkyl; and

with the proviso that: (a) when R^4 is attached to nitrogen, it is not halo, cyano or nitro; and (b) one of E, D and F must be nitrogen or substituted nitrogen, and only one of E, D and F can be nitrogen or substituted nitrogen;

F2
cont

Z is NH, oxygen, sulfur, -N(C₁-C₄ alkyl), -NC(=O)(C₁-C₂ alkyl), NC(=O)O(C₁-C₂alkyl) or CR¹³R¹⁴ wherein R¹³ and R¹⁴ are independently selected from hydrogen, trifluoromethyl and methyl with the exception that one of R¹³ and R¹⁴ can be cyano;
or a pharmaceutically acceptable salt of such compound.
